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********** STN Columbus **********
FILE 'HOME' ENTERED AT 12:43:37 ON 23 SEP 1999
=> file .bio
=> e porro m/au
=> s e3-e9,e13
L1      205 ("PORRO M"/AU OR "PORRO M A"/AU OR "PORRO M C"/AU
OR "PORRO M
        E"/AU OR "PORRO M G"/AU OR "PORRO M N"/AU OR "PORRO
M NAZZARO"/A
        U OR "PORRO MASSIMO"/AU)

=> s l1 and (peptide? or polypeptide? or lps or lipopolysaccharide?)
L2      51 L1 AND (PEPTIDE? OR POLYPEPTIDE? OR LPS OR
LIPOPOLYSACCHARIDE?)

=> s l1 and endotoxin?
L3      27 L1 AND ENDOTOXIN?

=> s l2 or l3
L4      51 L2 OR L3

=> s l5 and (endotoxin? or lps or lipopolysaccharide?)
L6      17 L5 AND (ENDOTOXIN? OR LPS OR
LIPOPOLYSACCHARIDE?)

=> d l6 1-17
L6  ANSWER 1 OF 17 CAPLUS  COPYRIGHT 1999 ACS
AN  1998:412126 CAPLUS
DN  129:188002
TI  Natural and synthetic ***polypeptides*** that recognize the conserved
    lipid A binding site of ***lipopolysaccharides***
AU  ***Porro, Massimo*** ; Rustici, Alessandro; Velucchi, Massimo;
Agnello,
    Davide; Villa, Pia; Ghezzi, Pietro
CS  Biosynth Research Laboratories, Siena, 53040, Italy
SO  Prog. Clin. Biol. Res. (1998), 397(Endotoxin and Sepsis), 315-325
    CODEN: PCBRD2; ISSN: 0361-7742
PB  Wiley-Liss, Inc.
DT  Journal; General Review
LA  English

L6  ANSWER 2 OF 17 CAPLUS  COPYRIGHT 1999 ACS
AN  1998:344326 CAPLUS
DN  129:27010
TI  Combined use of anti- ***endotoxin*** synthetic ***peptides***
and
    of anti- ***endotoxin*** antibodies for the prophylaxis and treatment
    of endotoxicosis and septic shock
IN  ***Porro, Massimo***
PA  Biosynth S.r.l., Italy
SO  Eur. Pat. Appl., 5 pp.
    CODEN: EPXXDW
DT  Patent
LA  English
FAN.CNT 1
    PATENT NO.      KIND  DATE        APPLICATION NO.  DATE
    --------------  ----  ------      --------------   --------
PI  EP 842666       A2    19980520    EP 1997-203526   19971112
      R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
PT,
         IE, SI, LT, LV, FI, RO
PRAI IT 1996-MI2354  19961113

L6  ANSWER 3 OF 17 CAPLUS  COPYRIGHT 1999 ACS
AN  1997:807227 CAPLUS
DN  128:74066
TI  A model of Neisseria meningitidis vaccine based on ***LPS***
micelles
    detoxified by synthetic anti- ***endotoxin*** ***peptides***
AU  Velucchi, M.; Rustici, A.; Meazza, C.; Villa, P.; Ghezzi, P.; Tsai, C-M.;
    ***Porro, M.***
CS  BiosYnth Research Laboratories, Rapolano Terme, Siena, Italy
SO  J. Endotoxin Res. (1997), 4(4), 261-272
    CODEN: JENREB; ISSN: 0968-0519
PB  Churchill Livingstone
DT  Journal
LA  English

L6  ANSWER 4 OF 17 CAPLUS  COPYRIGHT 1999 ACS
AN  1997:539250 CAPLUS
DN  127:172534
TI  Highly basic ***peptides*** that neutralize the toxicity of lipid A
    for use in the treatment of septic shock
IN  ***Porro, Massimo***
PA  Biosynth S.r.L., Italy
SO  U.S., 14 pp. Cont.-in-part of U.S. 5,358,933.
    CODEN: USXXAM
DT  Patent
LA  English
FAN.CNT 5
    PATENT NO.      KIND  DATE        APPLICATION NO.  DATE
    --------------  ----  ------      --------------   --------
PI  US 5652211      A     19970729    US 1993-97830    19930726
    US 5371186      A     19941206    US 1992-819893   19920116
    US 5358933      A     19941025    US 1993-49871    19930419
    WO 9503327      A2    19950202    WO 1994-EP2413   19940721
    WO 9503327      A3    19950504
      W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI,
GB,
         GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN,
MW,
         NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ,
VN
      RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU,
MC,
         NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN,
TD, TG
    AU 9474602      A1    19950220    AU 1994-74602    19940721
    AU 683920       B2    19971127
    EP 711307       A1    19960515    EP 1994-924272   19940721
      R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT,
SE
    JP 09503489     T2    19970408    JP 1994-504948   19940721
PRAI US 1991-658744  19910211
    US 1992-819893  19920116
    US 1993-49871   19930419
    US 1993-97830   19930726
    WO 1994-EP2413  19940721

L6  ANSWER 5 OF 17 CAPLUS  COPYRIGHT 1999 ACS
AN  1997:175746 CAPLUS
DN  126:233139
TI  Inhibition of ***LPS*** -induced systemic and local TNF production by
a
    synthetic anti- ***endotoxin*** ***peptide*** (SAEP-2)
AU  Demitri, M. T.; Velucchi, M.; Bracci, L.; Rustici, A.; ***Porro, M.***
    ; Villa, P.; Ghezzi, P.
CS  Istituto Richerche Farmacologiche, Mario Negri, Milan, Italy
SO  J. Endotoxin Res. (1996), 3(6), 445-454
    CODEN: JENREB; ISSN: 0968-0519
PB  Churchill Livingstone
DT  Journal
LA  English

L6  ANSWER 6 OF 17 CAPLUS  COPYRIGHT 1999 ACS
AN  1995:615187 CAPLUS
DN  123:27638
TI  ***Peptides*** for neutralizing the toxicity of lipid A
IN  ***Porro, Massimo***
PA  Biosynth S.r.L., Italy
SO  PCT Int. Appl., 24 pp.
    CODEN: PIXXD2
DT  Patent
LA  English
FAN.CNT 5
    PATENT NO.      KIND  DATE        APPLICATION NO.  DATE
    --------------  ----  --------    --------------   --------
PI  WO 9503327      A2    19950202    WO 1994-EP2413   19940721
    WO 9503327      A3    19950504
      W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI,
GB,
         GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN,
MW,
         NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ,
VN
      RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU,
MC,
         NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN,
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TD, TG
US 5652211 A 19970729 US 1993-97830 19930726
AU 9474602 A1 19950220 AU 1994-74602 19940721
AU 683920 B2 19971127
EP 711307 A1 19960515 EP 1994-924272 19940721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
JP 09503489 T2 19970408 JP 1994-504948 19940721
PRAI US 1993-97830 19930726
US 1991-658744 19910211
US 1992-819893 19920116
US 1993-49871 19930419
WO 1994-EP2413 19940721

L6 ANSWER 7 OF 17 CAPLUS COPYRIGHT 1999 ACS
AN 1995:354473 CAPLUS
DN 122:133872
TI Preparation of ***peptides*** for detoxification of bacterial ***endotoxins*** and for the prevention and treatment of septic shock.
IN ***Porro, Massimo***
PA Biosynth S.r.l., Italy
SO U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 658,744, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5371186	A	19941206	US 1992-819893	19920116
WO 9314115	A1	19930722	WO 1992-EP1060	19920514
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MW, NL, NO, RO, RU, SD, SE, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9216914	A1	19930803	AU 1992-16914	19920514
AU 665945	B2	19960125		
EP 623144	A1	19941109	EP 1992-910229	19920514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
HU 69707	A2	19950928	HU 1994-1970	19920514
US 5652211	A	19970729	US 1993-97830	19930726
FI 9403396	A	19940715	FI 1994-3396	19940715
US 5589459	A	19961231	US 1994-280397	19940726

PRAI US 1991-658744 19910211
US 1992-819893 19920116
WO 1992-EP1060 19920514
US 1993-49871 19930419
OS MARPAT 122:133872

L6 ANSWER 8 OF 17 CAPLUS COPYRIGHT 1999 ACS
AN 1994:698634 CAPLUS
DN 121:298634
TI Molecular requirements of ***peptide*** structures binding to the lipid-A region of bacterial ***endotoxins***
AU Velucchi, Massimo; Rustici, Alessandro; ***Porro, Massimo***
CS BioYnth Res. Lab., Zona Industriale, Siena, 53040, Italy
SO Vaccines 94: Mod. Approaches New Vaccines Incl. Prev. AIDS, [Annu. Meet.], 11th (1994), Meeting Date 1993, 141-6. Editor(s): Norrby, Erling. Publisher: Cold Spring Harbor Lab. Press, Cold Spring Harboy, N.Y.
CODEN: 60PMAJ
DT Conference
LA English

L6 ANSWER 9 OF 17 CAPLUS COPYRIGHT 1999 ACS
AN 1994:105011 CAPLUS
DN 120:105011
TI Synthetic lipid A glycoconjugate antigens for use in vaccines
IN ***Porro, Massimo***
PA American Cyanamid Co., USA
SO Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 570682	A1	19931124	EP 1993-104369	19930317
EP 570682	B1	19970723		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 155790	E	19970815	AT 1993-104369	19930317
ES 2104984	T3	19971016	ES 1993-104369	19930317
CA 2095588	AA	19931108	CA 1993-2095588	19930505
NO 9301655	A	19931108	NO 1993-1655	19930506
NO 180234	B	19961202		
NO 180234	C	19970312		
AU 9338419	A1	19931111	AU 1993-38419	19930506
AU 664609	B2	19951123		
JP 06041200	A2	19940215	JP 1993-129939	19930506

PRAI US 1992-879403 19920507
OS MARPAT 120:105011

L6 ANSWER 10 OF 17 CAPLUS COPYRIGHT 1999 ACS
AN 1993:574225 CAPLUS
DN 119:174225
TI Synthetic ***peptides*** for detoxification of bacterial ***endotoxins*** and treatment of septic shock
IN ***Porro, Massimo***
PA Italy
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9314115	A1	19930722	WO 1992-EP1060	19920514
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MW, NL, NO, RO, RU, SD, SE, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
US 5371186	A	19941206	US 1992-819893	19920116
AU 9216914	A1	19930803	AU 1992-16914	19920514
AU 665945	B2	19960125		
EP 623144	A1	19941109	EP 1992-910229	19920514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
FI 9403396	A	19940715	FI 1994-3396	19940715

PRAI US 1992-819893 19920116
US 1991-658744 19910211
WO 1992-EP1060 19920514

L6 ANSWER 11 OF 17 CAPLUS COPYRIGHT 1999 ACS
AN 1993:463064 CAPLUS
DN 119:63064
TI Synthetic ***peptides*** for detoxification of bacterial ***endotoxins*** and for prevention and treatment of septic shock
IN ***Porro, Massimo***
PA Italy
SO S. African, 40 pp.
CODEN: SFXXAB
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI ZA 9200943	A	19921125	ZA 1992-943	19920210

PRAI US 1991-658744 19910211

L6 ANSWER 12 OF 17 CAPLUS COPYRIGHT 1999 ACS
AN 1993:204745 CAPLUS
DN 118:204745
TI Molecular mapping and detoxification of the lipid A binding site by synthetic ***peptides***
AU Rustici, Alessandro; Velucchi, Massimo; Faggioni, Raffaella; Sironi, Marina; Ghezzi, Pietro; Quataert, Sally; Green, Bruce; ***Porro,*** *** Massimo***
CS Biosynth Res. Lab., Siena, 53040, Italy
SO Science (Washington, D. C., 1883-) (1993), 259(5093), 361-5
CODEN: SCIEAS; ISSN: 0036-8075
DT Journal
LA English

L6 ANSWER 13 OF 17 MEDLINE
AN 94207659 MEDLINE
DN 94207659
TI Structural basis of ***endotoxin*** recognition by natural

polypeptides .
AU ***Porro M***
CS BiosYnth Research Laboratories, Rapolano Terme, Siena, Italy..
SO TRENDS IN MICROBIOLOGY, (1994 Mar) 2 (3) 65-6; discussion 66-7.
Ref: 17
Journal code: B1N. ISSN: 0966-842X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199407

L6 ANSWER 14 OF 17 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:385462 BIOSIS
DN PREV199800385462
TI Natural and synthetic ***polypeptides*** that recognize the conserved lipid A binding site of ***lipopolysaccharides*** .
AU ***Porro, Massimo (1)*** ; Rustici, Alessandro (1); Velucchi, Massimo
(1); Agnello, Davide; Villa, Pia; Ghezzi, Pietro
CS (1) BiosYnth Res. Lab., 53040 Rapolano Terme, Siena Italy
SO Levin, J. [Editor]; Pollack, M. [Editor]; Yokochi, T. [Editor]; Nakano, M. [Editor]. Progress in Clinical and Biological Research, (1998) Vol. 397, pp. 315-325. Progress in Clinical and Biological Research; Endotoxin and sepsis: Molecular mechanisms of pathogenesis, host resistance, and therapy.
Publisher: Wiley-Liss, Inc. 605 Third Avenue, New York, New York 10158-0012, USA.
Meeting Info.: 4th Conference of the International Endotoxin Society Nagoya, Japan October 23-27, 1996 International Endotoxin Society . ISSN: 0361-7742. ISBN: 0-471-19432-8.
DT Book; Conference
LA English

L6 ANSWER 15 OF 17 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1997:49972 BIOSIS
DN PREV199799349175
TI Natural and synthetic ***polypeptides*** that recognize the conserved lipid A binding site of ***lipopolysaccharides*** .
AU ***Porro, Massimo*** ; Rustici, Alessandro; Velucchi, Massimo
CS BiosYnth Res. Lab., Rapolano Terme, Siena Italy
SO Journal of Endotoxin Research, (1996) Vol. 3, No. SUPPL. 1, pp. 11.
Meeting Info.: Fourth International Endotoxin Society Conference Nagoya, Japan October 22-25, 1996
ISSN: 0968-0519.
DT Conference; Abstract
LA English

L6 ANSWER 16 OF 17 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1994:423370 BIOSIS
DN PREV199497436370
TI Molecular requirements of ***peptide*** structure binding to the lipid-A region of bacterial ***endotoxins*** .
AU Velucchi, Massimo; Rustici, Alessandro; ***Porro, Massimo***
CS Biosynth Res. Lab., Zona Industriale, Rapolano Terme, Siena 53040 Italy
SO Norrby, E. [Editor]; Brown, F. [Editor]; Chanock, R. M. [Editor]; Ginsberg, H. S. [Editor]. Vaccines (Cold Spring Harbor), (1994) Vol. 94, pp. 141-146. Vaccines (Cold Spring Harbor); Modern approaches to new vaccines including prevention of AIDS.
Publisher: Cold Spring Harbor Laboratory Press 10 Skyline Drive, Plainview, New York 11803, USA.
Meeting Info.: Eleventh Annual Meeting on Modern Approaches to New Vaccines Cold Spring Harbor, New York, USA September 1993
ISSN: 0899-4056. ISBN: 0-87969-434-3.
DT Book; Conference
LA English

L6 ANSWER 17 OF 17 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 94159103 EMBASE
DN 1994159103
TI Synthetic ***peptides*** for detoxification of bacterial ***endotoxins*** and treatment of septic shock.
AU ***Porro M.***
SO Expert Opinion on Therapeutic Patents, (1994) 4/5 (559).
ISSN: 0962-2594 CODEN: EOTPEG
CY United Kingdom
DT Journal; (Short Survey)
FS 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LA English

=> d l6 1-17 ti,ab

L6 ANSWER 1 OF 17 CAPLUS COPYRIGHT 1999 ACS
TI Natural and synthetic ***polypeptides*** that recognize the conserved lipid A binding site of ***lipopolysaccharides***
AB A review with .apprx.25 refs. The authors review their work on various natural and synthetic ***polypeptides*** that recognize the conserved lipid A binding site of ***lipopolysaccharides*** and in particular talk about in vivo and in vitro assays demonstrating the ability of nociceptin to neutralize ***lipopolysaccharide*** activity. The results suggest that nociceptin might be a potential target of ***LPS*** in the central and peripheral nervous system. Its capability to interact with ***LPS*** , through lipid A, might work as a recognition system alerting the host's defenses on the basis of an imbalance in the equil. nociceptin/nociceptor, therefore serving as a physiol. defense against the early biol. effects which follow an ***LPS*** insult.

L6 ANSWER 2 OF 17 CAPLUS COPYRIGHT 1999 ACS
TI Combined use of anti- ***endotoxin*** synthetic ***peptides*** and
of anti- ***endotoxin*** antibodies for the prophylaxis and treatment of endotoxicosis and septic shock
AB Methods and compns. for neutralizing ***endotoxin*** and for the prophylaxis and treatment of endotoxicosis and septic shock are disclosed, which comprise the use of ***peptides*** specifically binding to the conserved ***endotoxin*** structure (Lipid A), and antibodies specifically binding to the antigenic determinants in the ***endotoxin*** core structure of different genera of Gram-neg. bacteria.

L6 ANSWER 3 OF 17 CAPLUS COPYRIGHT 1999 ACS
TI A model of Neisseria meningitidis vaccine based on ***LPS*** micelles
detoxified by synthetic anti- ***endotoxin*** ***peptides***
AB The authors describe a vaccine model based on detoxified ***endotoxin***
(***LPS***) conserving the supramol. structure of micelles. Detoxification of ***LPS*** from Neisseria meningitidis group A, strain A1 (***LPS*** A1), was achieved by complex formation with synthetic anti- ***endotoxin*** ***peptide*** (SAEP 2) binding to the lipid A moiety of ***LPS*** A1 with high affinity. Following s.c. injection in SW mice, ***LPS*** A1/SAEP 2 complex induced high titers
of boostable IgG antibodies against the immunotype determinants of ***LPS*** A1, cross-reactive with group B ***LPS*** in either purified or cell-assocd. form. These antibodies were able to functionally fix and activate homologous and heterologous species of complement after binding to ***LPS*** A1-coated sheep erythrocytes. None of the IgG antibodies induced were specific for lipid A or SAEP 2 and none of the IgG antibodies cross-reacted with heterologous ***LPS*** . The purified IgG polyclonal antibodies significantly inhibited serum TNF prodn. in CD1 mice i.v. challenged by homologous but not heterologous ***LPS*** . The immunogenic properties of ***LPS*** A1/SAEP 2 complex, investigated by the kinetic, magnitude and sub-isotype compn. of the polyclonal antibodies induced, were comparable to those of a glycoconjugate obtained by covalent binding of ***LPS*** A1, detoxified by SAEP 2, to BSA working as a T-cell dependent carrier protein. The results obtained suggest that ***LPS*** behaves in vivo as a T-cell dependent antigen. The strategy of properly delivering to the immune system of mammals, non-toxic ***LPS*** fully expressing its supramol. antigenic structure, represents a novel approach for development of a new generation of R- and S- ***LPS*** /SAEP complex-based vaccines
for prophylaxis of specific Gram-neg. infections leading to sepsis and endotoxemia.

L6 ANSWER 4 OF 17 CAPLUS COPYRIGHT 1999 ACS
TI Highly basic ***peptides*** that neutralize the toxicity of lipid A for use in the treatment of septic shock
AB Repetitive highly basic ***peptides*** that counteract the toxicity of lipid A and that can be used in the treatment of septic shock are

described. These ***peptides*** have the formula: (R1)n (R1 = Lys or Arg, n >6); (R1R3)m (R3 = Val, Leu, Ile, Tyr, Phe, Trp, m >2); (R1R5R6)p (R5, R6 = independently Val, Leu, Ile, Tyr, Phe, Trp; p .gtoreq.2). Several of these ***peptides*** are derived from known ***endotoxin*** -binding proteins. The compns. of the invention bind Lipid-A of ***endotoxins*** . These ***peptides*** can be used in vaccine formulations to prevent adverse reactions to lipid A. Characterization of the inhibitory properties of several of these ***peptides*** is reported.

L6 ANSWER 5 OF 17 CAPLUS COPYRIGHT 1999 ACS
TI Inhibition of ***LPS*** -induced systemic and local TNF production by a
synthetic anti- ***endotoxin*** ***peptide*** (SAEP-2)
AB ***Lipopolysaccharide*** (***LPS***) exerts its biol. activity through the lipid A moiety. We tested the efficiency in inhibiting TNF prodn. in sera and in tissues of mice and in the derma of rabbits challenged with ***LPS*** of a synthetic anti- ***LPS*** ***peptide*** (SAEP-2) previously shown to specifically detoxify the lipid A region of ***LPS*** on the basis of structural similarities with the antibiotic polymyxin B (PMXB). In mice, SAEP-2 (100 .mu.g/mouse, i.v.) injected with various schedules ('-30 to +10 min from ***LPS*** at 50 ng/mouse, i.v.) significantly inhibited serum TNF as well as liver, spleen and lung-assocd. TNF. In rabbits, SAEP-2 significantly inhibited TNF produced in dermal tissue and the resulting local hemorrhagic necrosis. The amt. of tissue-assocd. TNF released by ***LPS*** challenge in the mouse was up to 6 times that present in ther serum and inhibition by SAEP-2 or PMXB accounted for 75% of the total. Direct measurement of the binding kinetics by surface plasmon resonance and mol. filtration at equil. revealed that SAEP-2 and PMXB bind to ***LPS*** only in the presence of a significant amt. of water but that they are unable to bind ***LPS*** in undiluted serum. Altogether these findings strongly suggest that inhibition of ***LPS*** -induced TNF by SAEP-2 and PMXB may occur in tissues.

L6 ANSWER 6 OF 17 CAPLUS COPYRIGHT 1999 ACS
TI ***Peptides*** for neutralizing the toxicity of lipid A
AB A ***peptide*** compn. for neutralizing the toxicity of lipid A exhibits the formula: (1) (A)n (A= Lys, Arg; n=integer .gtoreq.7); (2) (AB)m (A as in (1); B= Val, Leu, Ile, Tyr, Phe, Try; m=integer .gtoreq.3); or (3) (ABC)p (A=Lys, Arg; B, C=Leu, Ile, Tyr, Phe, Try; p=integer .gtoreq.2). The compn. binds lipid-A of ***endotoxins*** and provides therapeutic and prophylactic uses. Novel 29 ***peptides*** capable of neutralizing the toxicity of lipid A are provided and their use on treating septic shock is claimed.

L6 ANSWER 7 OF 17 CAPLUS COPYRIGHT 1999 ACS
TI Preparation of ***peptides*** for detoxification of bacterial ***endotoxins*** and for the prevention and treatment of septic shock.
AB R1-(X1-X2-X3)n-R (R, R1 = H, amino acid residue, fatty acid residue; X1 =
Lys, Arg, His; X2 = Phe, Tyr, Trp; X3 = Leu, Ile, Val; n = 1-100), and polymeric and cyclic analogs thereof, were prepd. Title ***peptides*** are used for the prevention and/or treatment of septic shock, for the detection of ***endotoxin*** , and for the prepn. of antigenic complexes of Lipid A. Thus, title compd. (I), prepd. by solid phase synthesis, at 0.1 mg i.v. gave a 40% survival rate in ***endotoxin*** -sensitive mice challenged with 1 .mu.g E. coli ***endotoxin*** , vs. 5% for untreated controls.

L6 ANSWER 8 OF 17 CAPLUS COPYRIGHT 1999 ACS
TI Molecular requirements of ***peptide*** structures binding to the lipid-A region of bacterial ***endotoxins***
AB The binding of selected ***peptides*** to lipid A of heterologous ***lipopolysaccharides*** was assessed and measured by the value of selectivity, which expresses the ratio between the affinity const. value of Polymyxin B and that of each synthetic ***peptide*** in competition anal. Both the ref. and the synthetic ***peptides*** with a value of .gtoreq.0.75 Rc/h were able to inhibit competitively the lipid A-induced hemorrhagic necrosis in rabbits at doses as high as 75-125 .mu.g/mL of ***LPS*** .

L6 ANSWER 9 OF 17 CAPLUS COPYRIGHT 1999 ACS
TI Synthetic lipid A glycoconjugate antigens for use in vaccines
AB Synthetic glycoconjugate antigens I (P1 = H, phosphate; R2 = C1-4 alkyl; P2 = H, Pr, allyl, phosphate; n = 1-30; Q = carrier protein or ***peptide***) are disclosed for use in vaccines for prophylaxis of septic shock caused by bacterial ***endotoxin*** . Also disclosed are methods of prepg. the glycoconjugates. Thus, propyl-6-O-(2-acetamido-2-deoxy-.beta.-D-glucopyranosyl)-2-amino-2-deoxy-.alpha.-D-glucopyranoside was prepd. and further reacted with adipic acid bis-succinimidyl ester, and the product was conjugated with carrier protein CRM197. Glycoconjugate-induced IgG immune response in rabbits was detd.

L6 ANSWER 10 OF 17 CAPLUS COPYRIGHT 1999 ACS
TI Synthetic ***peptides*** for detoxification of bacterial ***endotoxins*** and treatment of septic shock
AB The novel ***peptides*** are R1-(A-B-C)n-R, wherein R1 and R are independently H or an amino acid residue or a fatty acid residue; A = Lys, Arg, or His; B = Phe, Tyr, or Trp; C = Leu, Ile, or Val; and n = 1-100. The ***peptides*** are used for prevention or treatment of septic shock, for the detection of ***endotoxin*** , and for prepn. of a safe antigenic complex of lipid A for producing anti-lipid A antibody.

L6 ANSWER 11 OF 17 CAPLUS COPYRIGHT 1999 ACS
TI Synthetic ***peptides*** for detoxification of bacterial ***endotoxins*** and for prevention and treatment of septic shock
AB The title ***peptides*** , e.g. Lys-Phe-Leu-contg. ***peptides*** (I), are effective in the treatment of septic shock by binding with the lipid A moiety of ***endotoxins*** . The ***peptides*** are also useful as a diagnostic probe for detection and quantitation of ***endotoxin*** in blood. The activity of the ***peptides*** were confirmed by the direct microprecipitin assay with Bacillus pertussis lipid A and ***lipopolysaccharide*** . Actinomycin D-sensitized mice were i.v. treated with I and challenged by i.p. injection of Escherichia coli ***endotoxin*** ; a survival rate after 7 days was 40%, compared to 30% and 5% for polymixin B-treated control group and saline-treated control group, resp.

L6 ANSWER 12 OF 17 CAPLUS COPYRIGHT 1999 ACS
TI Molecular mapping and detoxification of the lipid A binding site by synthetic ***peptides***
AB ***Endotoxin*** [***lipopolysaccharide*** (***LPS***)], the major antigen of the outer membrane of gram-neg. bacteria, consists of a variable-size carbohydrate chain that is covalently linked to N,O-acylated .beta.-1,6-D-glucosamine disaccharide 1,4'-bisphosphate (lipid A). The toxic activity of ***LPS*** resides in the lipid A structure. The structural features of synthetic ***peptides*** that bind to lipid A with high affinity, detoxify ***LPS*** in vitro, and prevent ***LPS*** -induced cytokine release and lethality in vivo were defined. The binding thermodn. were comparable to that of an antigen-antibody reaction. Such synthetic ***peptides*** may provide a strategy for prophylaxis and treatment of ***LPS*** -mediated diseases.

L6 ANSWER 13 OF 17 MEDLINE
TI Structural basis of ***endotoxin*** recognition by natural ***polypeptides*** .

L6 ANSWER 14 OF 17 BIOSIS COPYRIGHT 1999 BIOSIS
TI Natural and synthetic ***polypeptides*** that recognize the conserved lipid A binding site of ***lipopolysaccharides*** .

L6 ANSWER 15 OF 17 BIOSIS COPYRIGHT 1999 BIOSIS
TI Natural and synthetic ***polypeptides*** that recognize the conserved lipid A binding site of ***lipopolysaccharides*** .

L6 ANSWER 16 OF 17 BIOSIS COPYRIGHT 1999 BIOSIS
TI Molecular requirements of ***peptide*** structure binding to the lipid-A region of bacterial ***endotoxins*** .

L6 ANSWER 17 OF 17 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
TI Synthetic ***peptides*** for detoxification of bacterial ***endotoxins*** and treatment of septic shock.

=> s (endotoxin? or lps or lipopolysaccharide?)(10n)(peptide? or polypeptide?)

L7 2388 (ENDOTOXIN? OR LPS OR LIPOPOLYSACCHARIDE?)(10N)(PEPTIDE? OR POLYPEPTIDE?)

=> s l7 and saep?
L8 7 L7 AND SAEP?

=> s l8 not l6
L9 5 L8 NOT L6

=> d l9 1-5
L9 ANSWER 1 OF 5 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:48059 BIOSIS
DN PREV199800048059
TI A model of Neisseria meningitidis vaccine based on ***LPS*** micelles
detoxified by synthetic anti- ***endotoxin*** ***peptides*** .
AU Velucchi, M.; Rustici, A.; Meazza, C.; Villa, P.; Ghezzi, P.; Tsai, C.-M.; Porro, M. (1)
CS (1) BiosYnth Res. Lab., 53040 Rapolano Terme, Siena Italy
SO Journal of Endotoxin Research, (Aug., 1997) Vol. 4, No. 4, pp. 261-272.
ISSN: 0968-0519.
DT Article
LA English

L9 ANSWER 2 OF 5 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 97353996 EMBASE
DN 1997353996
TI A model of Neisseria meningitidis vaccine based on ***LPS*** micelles
detoxified by synthetic anti- ***endotoxin*** ***peptides*** .
AU Velucchi M.; Rustici A.; Meazza C.; Villa P.; Ghezzi P.; Tsai C.-M.; Porro
M.
CS Dr. M. Porro, Biosynth Research Laboratories, 53040 Rapolano Terme, Siena,
Italy
SO Journal of Endotoxin Research, (1997) 4/4 (261-272).
Refs: 46
ISSN: 0968-0519 CODEN: JENREB
CY United Kingdom
DT Journal; Article
FS 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English

L9 ANSWER 3 OF 5 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 97049157 EMBASE
DN 1997049157
TI Inhibition of LPS-induced systemic and local TNF production by a synthetic
anti- ***endotoxin*** ***peptide*** (***SAEP*** -2).
AU Demitri M.T.; Velucchi M.; Bracci L.; Rustici A.; Porro M.; Villa P.; Ghezzi P.
CS Dr. M. Porro, BiosYnth srl, Zona Industriale-Loc. Sentino, 53040 Rapolano
Terme, Siena, Italy
SO Journal of Endotoxin Research, (1996) 3/6 (445-454).
Refs: 32
ISSN: 0968-0519 CODEN: JENREB
CY United Kingdom
DT Journal; Article
FS 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English

L9 ANSWER 4 OF 5 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 97:893671 SCISEARCH
GA The Genuine Article (R) Number: YH658
TI A model of Neisseria meningitidis vaccine based on ***LPS*** micelles
detoxified by synthetic anti- ***endotoxin*** ***peptides***
AU Velucchi M; Rustici A; Meazza C; Villa P; Ghezzi P; Tsai C M; Porro M (Reprint)
CS BIOS YNTH RES LABS, I-53040 RAPOLANO TERME, SIENA, ITALY (Reprint); BIOS
YNTH RES LABS, I-53040 RAPOLANO TERME, SIENA, ITALY; IST RIC FARMACOL
MARIO NEGRI, MILAN, ITALY; CNR, CELLULAR & MOL PHARMACOL CTR, I-20133
MILAN, ITALY; US FDA, DEPT HLTH & HUMAN SERV, CTR BIOL EVALUAT & RES,
BETHESDA, MD 20014
CYA ITALY; USA
SO JOURNAL OF ENDOTOXIN RESEARCH, (AUG 1997) Vol. 4, No. 4, pp. 261-272.
Publisher: CHURCHILL LIVINGSTONE, JOURNAL PRODUCTION DEPT, ROBERT
STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH EH1 3AF,
MIDLOTHIAN, SCOTLAND.
ISSN: 0968-0519.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 45
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L9 ANSWER 5 OF 5 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 97:116400 SCISEARCH
GA The Genuine Article (R) Number: WF094
TI Inhibition of LPS-induced systemic and local TNF production by a synthetic
anti- ***endotoxin*** ***peptide*** (***SAEP*** -2)
AU Demitri M T; Velucchi M; Bracci L; Rustici A; Porro M (Reprint); Villa P;
Ghezzi P
CS ZORA IND LOC SENTINO, I-53040 RAPOLANO TERNE, SIENA, ITALY (Reprint); IST
RIC FARMACOL MARIO NEGRI, MILAN, ITALY; CNR, CELLULAR & MOL PHARMACOL CTR,
I-20133 MILAN, ITALY; UNIV SIENA, DEPT BIOL MOL, I-53100 SIENA, ITALY;
BIOSYNTH SRL, SIENA, ITALY
CYA ITALY
SO JOURNAL OF ENDOTOXIN RESEARCH, (DEC 1996) Vol. 3, No. 6, pp. 445-454.
Publisher: CHURCHILL LIVINGSTONE, JOURNAL PRODUCTION DEPT, ROBERT
STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH, MIDLOTHIAN,
SCOTLAND EH1 3AF.
ISSN: 0968-0519.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 32
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

=> s l7 and (cationic(3n)(peptide? or polypeptide?))
L10 97 L7 AND (CATIONIC(3N)(PEPTIDE? OR POLYPEPTIDE?))

=> s l11 not l6
L12 38 L11 NOT L6

=> d l12 1-38
L12 ANSWER 1 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1999:350378 CAPLUS
DN 131:129023
TI Production of .beta.-defensin antimicrobial peptides by the oral mucosa and salivary glands
AU Mathews, Michael; Jia, Hong Peng; Guthmiller, Janet M.; Losh, Garrett; Graham, Scott; Johnson, Georgia K.; Tack, Brian F.; McCray, Paul B., Jr.
CS Department of Periodontics and Dows Institute for Dental Research, University of Iowa Colleges of Medicine and Dentistry, Iowa City, IA, USA
SO Infect. Immun. (1999), 67(6), 2740-2745
CODEN: INFIBR; ISSN: 0019-9567
PB American Society for Microbiology
DT Journal
LA English

L12 ANSWER 2 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1999:214854 CAPLUS
DN 131:17975
TI Biological properties of structurally related .alpha.-helical ***cationic*** antimicrobial ***peptides***
AU Scott, Monisha G.; Yan, Hong; Hancock, Robert E. W.
CS Department of Microbiology and Immunology, University of British Columbia, Vancouver, BC, V6T 1Z3, Can.
SO Infect. Immun. (1999), 67(4), 2005-2009
CODEN: INFIBR; ISSN: 0019-9567
PB American Society for Microbiology

DT Journal
LA English

L12 ANSWER 3 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1999:210231 CAPLUS
DN 131:2579
TI The lipopolysaccharide outer core of Yersinia enterocolitica serotype 0:3 is required for virulence and plays a role in outer membrane integrity
AU Skurnik, Mikael; Venho, Reija; Bengoechea, Jose-Antonio; Moriyon, Ignacio
CS Department of Medical Biochemistry, University of Turku, Turku, 20520, Finland
SO Mol. Microbiol. (1999), 31(5), 1443-1462
CODEN: MOMIEE; ISSN: 0950-382X
PB Blackwell Science Ltd.
DT Journal
LA English

L12 ANSWER 4 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1999:167208 CAPLUS
DN 130:321746
TI Kinetics of the interaction of endotoxin with polymyxin B and its analogs: a surface plasmon resonance analysis
AU Thomas, Celestine J.; Surolia, Avadhesha
CS Molecular Biophysics Unit, Indian Institute of Science, Bangalore, 560 012, India
SO FEBS Lett. (1999), 445(2,3), 420-424
CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal
LA English

L12 ANSWER 5 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1999:113715 CAPLUS
DN 130:163167
TI Novel synthetic ***peptides*** with antimicrobial and ***endotoxin*** neutralizing properties for management of the sepsis syndrome
IN Appelmelk, Bernard Jan; Abraham, Philip Richard; Van Deventer, Sander Jan
Hendrik
PA Academisch Ziekenhuis Bij de Universiteit van Amsterdam, Neth.
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9906440	A1	19990211	WO 1997-NL449	19970731

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
OS MARPAT 130:163167

L12 ANSWER 6 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1999:38139 CAPLUS
DN 130:220289
TI Interaction of the cyclic antimicrobial ***cationic*** ***peptide*** bactenecin with the outer and cytoplasmic membrane
AU Wu, Manhong; Hancock, Robert E. W.
CS Department of Microbiology and Immunology, University of British Columbia, Vancouver, BC, V6T 1Z3, Can.
SO J. Biol. Chem. (1999), 274(1), 29-35
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English

L12 ANSWER 7 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1998:784259 CAPLUS
DN 130:152497
TI The ***lipopolysaccharide*** of Bordetella bronchiseptica acts as a protective shield against antimicrobial ***peptides***
AU Banemann, Andreas; Deppisch, Heike; Gross, Roy
CS Lehrstuhl fur Mikrobiologie, Theodor-Boveri-Institut, Biozentrum der Universitat Wurzburg, Wurzburg, D-97074, Germany
SO Infect. Immun. (1998), 66(12), 5607-5612
CODEN: INFIBR; ISSN: 0019-9567
PB American Society for Microbiology
DT Journal
LA English

L12 ANSWER 8 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1998:534878 CAPLUS
DN 129:156918
TI Treatment of ***endotoxin*** -associated disorders with ***cationic*** ***peptides***
IN Hancock, Robert E. W.; Piers, Kevin L.; Brown, Melissa H.; Kelly, Niamh
PA University of British Columbia, Can.
SO U.S., 37 pp. Cont.-in-part of U.S. Ser. No. 110,502, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5789377	A	19980804	US 1995-405234	19950313
US 5593866	A	19970114	US 1995-575052	19951220
WO 9628559	A1	19960919	WO 1996-IB431	19960313

W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

CA 2215362	AA	19960919	CA 1996-2215362	19960313
US 5688767	A	19971118	US 1996-614516	19960313
EP 815247	A1	19980107	EP 1996-911076	19960313

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, IE

JP 11503006	T2	19990323	JP 1996-527425	19960313
US 5707855	A	19980113	US 1996-770557	19961220

PRAI US 1992-933492 19920821
US 1993-110502 19930820
US 1995-405234 19950313
US 1995-575052 19951220
WO 1996-IB431 19960313

L12 ANSWER 9 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1998:515060 CAPLUS
DN 129:259188
TI Polymyxin-B stimulates tumor necrosis factor-.alpha. production by human peripheral blood mononuclear cells
AU Jaber, B. L.; Sundaram, S.; Neto, M. Cendoroglo; King, A. J.; Pereira, B. J. G.
CS Division of Nephrology, Department of Medicine, New England Medical Center Hospitals, Boston, MA, USA
SO Int. J. Artif. Organs (1998), 21(5), 269-273
CODEN: IJAODS; ISSN: 0391-3988
PB Wichtig Editore
DT Journal
LA English

L12 ANSWER 10 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1998:97201 CAPLUS
DN 128:238775
TI The therapeutic potential of ***cationic*** ***peptides***
AU Hancock, Robert E. W.
CS The University of British Columbia, Vancouver, BC, V6T 1Z3, Can.
SO Expert Opin. Invest. Drugs (1998), 7(2), 167-174
CODEN: EOIDER; ISSN: 0967-8298
PB Ashley Publications
DT Journal; General Review
LA English

L12 ANSWER 11 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1998:84494 CAPLUS
DN 128:158893
TI Removal of cytokine inducing substances by polymyxin-B immobilized polystyrene-derivative fibers during in vitro hemoperfusion of 10% human plasma containing Staphylococcus aureus challenge

AU Jaber, Bertrand L.; Barrett, Tyler W.; Neto, Miguel Cendoroglo; Sundaram,
Sumuk; King, Andrew J.; Pereira, Brian J. G.
CS Division of Nephrology, Department of Medicine, New England Medical Center
Hospitals, Boston, MA, 02111, USA
SO ASAIO J. (1998), 44(1), 48-53
CODEN: AJOUET; ISSN: 1058-2916
PB Lippincott-Raven Publishers
DT Journal
LA English

L12 ANSWER 12 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1997:736589 CAPLUS
DN 128:45750
TI Regulation of polymyxin resistance and adaptation to low-Mg2+ environments
AU Groisman, Eduardo A.; Kayser, Jason; Soncini, Fernando C.
CS Howard Hughes Medical Institute, Washington University School of Medicine,
St. Louis, MO, 63110, USA
SO J. Bacteriol. (1997), 179(22), 7040-7045
CODEN: JOBAAY; ISSN: 0021-9193
PB American Society for Microbiology
DT Journal
LA English

L12 ANSWER 13 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1997:546078 CAPLUS
DN 127:217166
TI Neutralization of the in vivo activity of E. coli-derived ***lipopolysaccharide*** by ***cationic*** ***peptides***
AU Brackett, Daniel J.; Lerner, Megan R.; Pereira, H. Anne
CS Departments of Surgery, Anesthesiology, and Pathology, Department of Veterans Affairs Medical Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA
SO Methods Mol. Biol. (Totowa, N. J.) (1997), 78(Antibacterial Peptide Protocols), 247-255
CODEN: MMBIED; ISSN: 1064-3745
PB Humana
DT Journal; General Review
LA English

L12 ANSWER 14 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1997:67477 CAPLUS
DN 126:72511
TI Antimicrobial ***cationic*** ***peptides***
IN Hancock, Robert E. W.; Karunartne, Nedra
PA University of British Columbia, Can.
SO PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9638473	A2	19961205	WO 1996-IB589	19960531
WO 9638473	A3	19970403		
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5877274	A	19990302	US 1995-460464	19950602
CA 2222599	AA	19961205	CA 1996-2222599	19960531
EP 842192	A2	19980520	EP 1996-916263	19960531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, IE, FI				
JP 11506326	T2	19990608	JP 1996-536344	19960531
PRAI US 1995-460464		19950602		
WO 1996-IB589		19960531		

OS MARPAT 126:72511

L12 ANSWER 15 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1997:24473 CAPLUS
DN 126:58833
TI A derivative of cationic antimicrobial protein attenuates lung injury by suppressing cell adhesion
AU Tasaka, Sadatomo; Ishizaka, Akitoshi; Urano, Tetsuya; Sayama, Koichi; Sakamaki, Fumio; Nakamura, Hidetoshi; Terashima, Takeshi; Waki, Yasuhiro;
Soejima, Kenzo; et al.
CS Departments of Medicine and Emergency Medicine, School of Medicine, Keio
University, Tokyo, Japan
SO Am. J. Respir. Cell Mol. Biol. (1996), 15(6), 738-744
CODEN: AJRBEL; ISSN: 1044-1549
PB American Lung Association
DT Journal
LA English

L12 ANSWER 16 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1996:718596 CAPLUS
DN 126:42284
TI Antiendotoxin activity of ***cationic*** ***peptide*** antimicrobial agents
AU Gough, Monisha; Hancock, Robert E. W.; Kelly, Niamh M.
CS Dep. Microbiol. Immunol. Pathol. Lab. Med., Univ. British Columbia, Vancouver, V6T 1Z3, UK
SO Infect. Immun. (1996), 64(12), 4922-4927
CODEN: INFIBR; ISSN: 0019-9567
PB American Society for Microbiology
DT Journal
LA English

L12 ANSWER 17 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1996:664931 CAPLUS
DN 125:294761
TI Manufacture with microorganisms of ***LPS*** -binding antibacterial ***cationic*** ***peptides*** conjugated with anionic ***peptides***
IN Hancock, Robert E. W.; Piers, Kevin L.; Brown, Melissa H.; Kelly, Niamh
PA University of British Columbia, Can.
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9628559	A1	19960919	WO 1996-IB431	19960313
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5789377	A	19980804	US 1995-405234	19950313
EP 815247	A1	19980107	EP 1996-911076	19960313
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, IE				
JP 11503006	T2	19990323	JP 1996-527425	19960313
PRAI US 1995-405234		19950313		
US 1992-933492		19920821		
US 1993-110502		19930820		
WO 1996-IB431		19960313		

L12 ANSWER 18 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1996:617707 CAPLUS
DN 125:269985
TI Brucella-Salmonella lipopolysaccharide chimeras are less permeable to hydrophobic probes and more sensitive to ***cationic*** ***peptides*** and EDTA than are their native Brucella sp. counterparts
AU Freer, Enrique; Moreno, Edgardo; Moriyon, Ignacio; Pizarro-Cerda, Javier;
Weintraub, Andrej; Gorvel, Jean-Pierre
CS Dep. Fisiologia, Facultad Medicina, Univ. Costa Rica, San Jose, Costa Rica
SO J. Bacteriol. (1996), 178(20), 5867-5876
CODEN: JOBAAY; ISSN: 0021-9193
DT Journal
LA English

L12 ANSWER 19 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1995:718963 CAPLUS
DN 123:167535
TI The outer membranes of Brucella spp. are resistant to bactericidal ***cationic*** ***peptides***
AU Martinez de Tejada, G.; Pizarro-Cerda, J.; Moreno, E.; Moriyon, I.
CS Dep. Microbiol., Univ. Navarra, Pamplona, Spain
SO Infect. Immun. (1995), 63(8), 3054-61
CODEN: INFIBR; ISSN: 0019-9567
DT Journal
LA English

L12 ANSWER 20 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1994:651065 CAPLUS
DN 121:251065
TI Improvement of outer membrane-permeabilizing and ***lipopolysaccharide*** -binding activities of an antimicrobial ***cationic*** ***peptide*** by C-terminal modification
AU Piers, Kevin L.; Brown, Melissa H.; Hancock, Robert E. W.
CS Dep. Microbiol. Immunol., Univ. British Columbia, Vancouver, BC, V6T 1Z3, Can.
SO Antimicrob. Agents Chemother. (1994), 38(10), 2311-16
CODEN: AMACCQ; ISSN: 0066-4804
DT Journal
LA English

L12 ANSWER 21 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1994:156972 CAPLUS
DN 120:156972
TI Molecular cloning of a putative homolog of proline/arginine-rich antibacterial peptides from porcine bone marrow
AU Pungercar, Joze; Strukelj, Borut; Kopitar, Gregor; Renko, Metka; Lenarcic, Brigita; Gubensek, Franc; Turk, Vito
CS Department of Biochemistry and Molecular Biology, Jozef Stefan Institute, Jamova 39, PO Box 100, Ljubljana, 61111, Slovenia
SO FEBS Lett. (1993), 336(2), 284-8
CODEN: FEBLAL; ISSN: 0014-5793
DT Journal
LA English

L12 ANSWER 22 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1994:124831 CAPLUS
DN 120:124831
TI Gene therapy by intramuscular injection of plasmid DNA: Studies on firefly luciferase gene expression in mice
AU Manthorpe, Marston; Cornefert-Jensen, Francine; Hartikka, Jukka; Felgner, Jiin; Rundell, Ann; Margalith, Michal; Dwarki, Varavani
CS VICAL, Inc., San Diego, CA, 92121, USA
SO Hum. Gene Ther. (1993), 4(4), 419-31
CODEN: HGTHE3; ISSN: 1043-0342
DT Journal
LA English

L12 ANSWER 23 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1993:400338 CAPLUS
DN 119:338
TI Interaction of basic amphiphilic polypeptide antimicrobials, gramicidin S, tyrocidine and efrapeptin, with endotoxic lipid A
AU David, S. A.; Balaram, P.; Mathan, V. I.
CS Dep. Gastrointest. Sci., Christian Med. Coll. Hosp. Vellore, Tamil Nadu, 632 004, India
SO Med. Microbiol. Lett. (1993), 2(1), 42-7
CODEN: MMLEEH; ISSN: 1018-4627
DT Journal
LA English

L12 ANSWER 24 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1991:404997 CAPLUS
DN 115:4997
TI Interactions between magainin 2 and Salmonella typhimurium outer membranes: effect of lipopolysaccharide structure
AU Rana, Fazale R.; Macias, Elizabeth A.; Sultany, Catherine M.; Modzrakowski, Malcolm C.; Blazyk, Jack
CS Coll. Osteopath. Med., Ohio Univ., Athens, OH, 45701, USA
SO Biochemistry (1991), 30(24), 5858-66
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English

L12 ANSWER 25 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1990:476378 CAPLUS
DN 113:76378
TI Primary structures and functions of anti- ***lipopolysaccharide*** factor and tachyplesin ***peptide*** found in horseshoe crab hemocytes
AU Muta, T.; Nakamura, T.; Furunaka, H.; Tokunaga, F.; Miyata, T.; Niwa, M.; Iwanaga, S.
CS Fac. Sci., Kyushu Univ. 33, Fukuoka, 812, Japan
SO Adv. Exp. Med. Biol. (1990), 256(Endotoxin), 273-85
CODEN: AEMBAP; ISSN: 0065-2598
DT Journal; General Review
LA English

L12 ANSWER 26 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1990:191448 CAPLUS
DN 112:191448
TI Interactions between Salmonella typhimurium ***lipopolysaccharide*** and the antimicrobial ***peptide*** , magainin 2 amide
AU Rana, Fazale R.; Sultany, Catherine M.; Blazyk, Jack
CS Coll. Osteopath. Med., Ohio Univ., Athens, OH, 45701, USA
SO FEBS Lett. (1990), 261(2), 464-7
CODEN: FEBLAL; ISSN: 0014-5793
DT Journal
LA English

L12 ANSWER 27 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1989:420596 CAPLUS
DN 111:20596
TI Outer membrane structure in smooth and rough strains of Salmonella typhimurium and their susceptibility to the antimicrobial peptides, magainins and defensins
AU Rana, Fazale; Blazyk, Jack
CS Coll. Osteopath. Med., Ohio Univ., Athens, OH, 45701, USA
SO Prog. Clin. Biol. Res. (1989), 292(Biol. Synth. Membr.), 77-85
CODEN: PCBRD2; ISSN: 0361-7742
DT Journal
LA English

L12 ANSWER 28 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1989:37483 CAPLUS
DN 110:37483
TI Polymyxin B suppresses the stimulating effect of pertussis vaccine on hematopoiesis in mice
AU Sanin, A. V.; Lapaeva, I. A.
CS NII Epidemiol. Mikrobiol., Moscow, USSR
SO Zh. Mikrobiol., Epidemiol. Immunobiol. (1988), (11), 19-23
CODEN: ZMEIAV; ISSN: 0372-9311
DT Journal
LA Russian

L12 ANSWER 29 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1987:532134 CAPLUS
DN 107:132134
TI Endotoxin-polymyxin complexes in an improved enzyme-linked immunosorbent assay for IgG antibodies in blood donor sera to gram-negative endotoxin core glycolipids
AU Scott, Boyd B.; Barclay, G. Robin
CS South East Scotland Reg. Blood Transfus. Cent., R. Infirm., Edinburgh, EH3 9HB, UK
SO Vox Sang. (1987), 52(4), 272-80
CODEN: VOSAAD; ISSN: 0042-9007
DT Journal
LA English

L12 ANSWER 30 OF 38 CAPLUS COPYRIGHT 1999 ACS
AN 1986:29996 CAPLUS
DN 104:29996
TI Dose-dependent reduction of lipopolysaccharide pyrogenicity by polymyxin B
AU Warner, Stephen J. C.; Mitchell, Duncan; Savage, Nerina; McClain, Elizabeth
CS Med. Sch., Univ. Witwatersrand, Johannesburg, 2193, S. Afr.
SO Biochem. Pharmacol. (1985), 34(22), 3995-8
CODEN: BCPCA6; ISSN: 0006-2952
DT Journal
LA English

L12 ANSWER 31 OF 38 MEDLINE
AN 89034158 MEDLINE
DN 89034158
TI Tachyplesin, a class of antimicrobial peptide from the hemocytes of the horseshoe crab (Tachypleus tridentatus). Isolation and chemical structure.
AU Nakamura T; Furunaka H; Miyata T; Tokunaga F; Muta T; Iwanaga S;

Niwa M;
Takao T; Shimonishi Y
CS Department of Biology, Faculty of Science, Kyushu University, Fukuoka, Japan..
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1988 Nov 15) 263 (32) 16709-13.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198902

L12 ANSWER 32 OF 38 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:261805 BIOSIS
DN PREV199800261805
TI Protective effects of a human 18-kilodalton cationic antimicrobial protein (CAP18)-derived peptide against murine endotoxemia.
AU Kirikae, Teruo (1); Hirata, Michimasa; Yamasu, Hiromi; Kirikae, Fumiko;
Tamura, Hiroshi; Kayama, Fumio; Nakatsuka, Keisuke; Yokochi, Takashi; Nakano, Masayasu
CS (1) Dep. Microbiol., Jichi Med. Sch., 3311-1 Yakushiji, Minamikawachi-machi, Tochigi-ken 329-0498 Japan
SO Infection and Immunity, (May, 1998) Vol. 66, No. 5, pp. 1861-1868.
ISSN: 0019-9567.
DT Article
LA English

L12 ANSWER 33 OF 38 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:69358 BIOSIS
DN PREV199800069358
TI ***Peptides*** corresponding to ***cationic*** sequences of ***LPS*** -binding proteins inhibit ***endotoxin*** -induced responses.
AU Arana, M. J.; Chinea, G.; Guerra, M.; Rodriguez, A.; Reyes, O.; Garay, H. E.; Padron, G.
CS Pharmaceutical Div., Cent. Genetic Engineering Biotechnol., PO Box 6996,
La Habana Cuba
SO Cytokine, (Nov., 1997) Vol. 9, No. 11, pp. 902.
Meeting Info.: Fifth Annual Conference of the International Cytokine Society Lake Tahoe, Nevada, USA November 9-13, 1997 International Cytokine
Society
. ISSN: 1043-4666.
DT Conference
LA English

L12 ANSWER 34 OF 38 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1997:417510 BIOSIS
DN PREV199799716713
TI Neutralization of the in vivo activity of E. coli-derived ***lipopolysaccharide*** by ***cationic*** ***peptides*** .
AU Brackett, Daniel J. (1); Lerner, Megan R.; Pereira, H. Anne
CS (1) Dep. Surgery, Univ. Oklahoma Health Sci. Cent., Oklahoma City, OK USA
SO Shafer, W. M. [Editor]. Methods in Molecular Biology, (1997) Vol. 78, pp.
247-255. Methods in Molecular Biology; Antibacterial peptide protocols.
Publisher: Humana Press Inc. Suite 808, 999 Riverview Drive, Totowa, New
Jersey 07512, USA.
ISSN: 0097-0816. ISBN: 0-89603-408-9.
DT Book
LA English

L12 ANSWER 35 OF 38 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1997:50048 BIOSIS
DN PREV199799349251
TI Comparison of structurally related ***cationic*** ***peptides*** in their ability to neutralize the biological activity of ***endotoxin*** .
AU Gough, Monisha; Kelly, Niamh; Hancock, R. E. W.
CS Canadian Bacterial Diseases Network, Univ. British Columbia, Vancouver, BC
Canada
SO Journal of Endotoxin Research, (1996) Vol. 3, No. SUPPL. 1, pp. 32.
Meeting Info.: Fourth International Endotoxin Society Conference Nagoya, Japan October 22-25, 1996
ISSN: 0968-0519.
DT Conference; Abstract; Conference
LA English

L12 ANSWER 36 OF 38 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1991:539570 BIOSIS
DN BR41:129305
TI INDUCTION OF ***CATIONIC*** ***PEPTIDES*** IN RABBIT ALVEOLAR
MACROPHAGE BY IMMUNOMODULATORS AND CYTOKINES.
AU ALLEGRETTO N; WARR G
CS BRISTOL-MYERS SQUIBB PRI, WALLINGFORD, CONN. 06492.
SO TWENTY-EIGHTH NATIONAL MEETING OF THE SOCIETY FOR LEUKOCYTE BIOLOGY AND
THE TWENTY-FIRST LEUKOCYTE CULTURE CONFERENCE, ASPEN, COLORADO, USA,
SEPTEMBER 28-OCTOBER 1, 1991. J LEUKOCYTE BIOL. (1991) 0 (SUPPL 2), 66.
CODEN: JLBIE7. ISSN: 0741-5400.
DT Conference
FS BR; OLD
LA English

L12 ANSWER 37 OF 38 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 75013852 EMBASE
DN 1975013852
TI Neutralization of the hemodynamic effects of endotoxin by polymyxin B.
AU Palmer J.D.; Rifkind D.
CS Dept. Pharmacol., Arizona Med. Cent., Univ. Arizona, Tucson, Ariz., United
States
SO Surgery Gynecology and Obstetrics, (1974) 138/5 (755-759).
CODEN: SGOBA
DT Journal
FS 037 Drug Literature Index
030 Pharmacology
006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
LA English

L12 ANSWER 38 OF 38 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 1998:330679 SCISEARCH
GA The Genuine Article (R) Number: ZJ781
TI Bactericidal activity of Lys49 and Asp49 myotoxic phospholipases A(2) from
Bothrops asper snake venom - Synthetic Lys49 myotoxin II-(115-129)-peptide
identifies its bactericidal region
AU Paramo L; Lomonte B (Reprint); PizarroCerda J; Bengoechea J A; Gorvel J P;
Moreno E
CS UNIV COSTA RICA, FAC MICROBIOL, INST CLODOMIRO PICADO, SAN JOSE, COSTA
RICA (Reprint); UNIV COSTA RICA, FAC MICROBIOL, INST CLODOMIRO PICADO, SAN
JOSE, COSTA RICA; UNIV NACL, ESCUELA MED VET, PROGRAMA INVEST ENFERMEDADES
TROP, HEREDIA, COSTA RICA; CTR IMMUNOL MARSEILLE LUMINY, MARSEILLE,
FRANCE; UNIV NAVARRA, DEPT MICROBIOL, E-31080 PAMPLONA, SPAIN
CYA COSTA RICA; FRANCE; SPAIN
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (APR 1998) Vol. 253, No. 2, pp. 452-461.
Publisher: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010.
ISSN: 0014-2956.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 50
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

=> d l12 1-37 ti,ab

L12 ANSWER 1 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Production of .beta.-defensin antimicrobial peptides by the oral mucosa and salivary glands
AB .beta.-Defensins are ***cationic*** ***peptides*** with broad-spectrum antimicrobial activity that are produced by epithelia at mucosal surfaces. Two human .beta.-defensins, HBD-1 and HBD-2, were discovered in 1995 and 1997, resp. However, little is known about the expression of HBD-1 or HBD-2 in tissues of the oral cavity and whether these proteins are secreted. Here, the authors characterized the expression of HBD-1 and HBD-2 mRNAs within the major salivary glands, tongue, gingiva, and buccal mucosa and detected .beta.-defensin peptides in salivary secretions. Defensin mRNA expression was quantitated by RNase protection assays. HBD-1 mRNA expression was detected in the gingiva, parotid gland, buccal mucosa, and tongue. Expression of HBD-2 mRNA was detected only in the gingival mucosa and was most abundant in tissues with assocd. inflammation. To test whether .beta.-defensin expression was inducible, gingival keratinocyte cell cultures were treated with interleukin-1.beta. (IL-1.beta.) or bacterial lipopolysaccharide (LPS) for 24 h. HBD-2 expression increased .apprx.16-fold with IL-1.beta. treatment and .apprx.5-fold in the presence of LPS. Western immunoblotting, liq. chromatog., and mass spectrometry were used to identify the HBD-1 and HBD-2 peptides in human saliva. Human .beta.-defensins are expressed in oral tissues, and the proteins are secreted in saliva; HBD-1 expression was constitutive, while HBD-2 expression was induced by IL-1.beta. and LPS. Human .beta.-defensins may play an important role in the innate defenses against oral microorganisms.

L12 ANSWER 2 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Biological properties of structurally related .alpha.-helical ***cationic*** antimicrobial ***peptides***
AB A series of .alpha.-helical ***cationic*** antimicrobial ***peptide*** variants with small amino acid changes was designed. Alterations in the charge, hydrophobicity, or length of the variant peptides did not improve the antimicrobial activity, and there was no statistically significant correlation between any of these factors and the MIC for Pseudomonas aeruginosa, Escherichia coli, or Salmonella typhimurium. Individual peptides demonstrated synergy with conventional antibiotics against antibiotic-resistant strains of P. aeruginosa. The peptides varied considerably in the ability to bind E. coli O111:B4 lipopolysaccharide (LPS), and this correlated significantly with their antimicrobial activity and ability to block LPS-stimulated tumor necrosis factor and interleukin-6 prodn. In general, the peptides studied here demonstrated a broad range of activities, including antimicrobial, antiendotoxin, and enhancer activities.

L12 ANSWER 3 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI The lipopolysaccharide outer core of Yersinia enterocolitica serotype 0:3 is required for virulence and plays a role in outer membrane integrity
AB Lipopolysaccharide (LPS) of Yersinia enterocolitica 0:3 has an inner core linked to both the O-antigen and to an outer core hexasaccharide that forms a branch. The biol. role of the outer core was studied using polar and non-polar mutants of the outer core biosynthetic operon. Anal. of O-antigen- and outer core-deficient strains suggested a crit. role for the outer core in outer membrane properties relevant in resistance to antimicrobial peptides and permeability to hydrophobic agents, and indirectly relevant in resistance to killing by normal serum. Wild-type bacteria but not outer core mutants killed intragastrically infected mice, and the i.v. LD was 104-fold higher for outer core mutants. After intragastric infection, outer core mutants colonized Peyer's patches and invaded mesenteric lymph nodes, spleen, and liver, and induced protective immunity against wild-type bacteria. In mice co-infected intragastrically with an outer core mutant-wild type mixt., both strains colonized Peyer's patches similarly during the first 2 days, but the mutant was much less efficient in colonizing deeper organs and was cleared faster from Peyer's patches. The results demonstrate that outer core is required for Y. enterocolitica 0:3 full virulence, and strongly suggest that it provides resistance against defense mechanisms (most probably those involving bactericidal peptides).

L12 ANSWER 4 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Kinetics of the interaction of endotoxin with polymyxin B and its analogs: a surface plasmon resonance analysis
AB Lipopolysaccharide, the invariant structural component of Gram-neg. bacteria, when present in minute amts. in the circulation in humans elicits 'endotoxic shock' syndrome, which is fatal in 60% of the cases. Polymyxin B (PMB), a cyclic ***cationic*** ***peptide*** , neutralizes the ***endotoxin*** , but also induces many harmful side effects. Many peptide-based drugs mimicking the activity of PMB have been synthesized in an attempt to reduce toxicity while still retaining the anti-endotoxic activity. The study attempts to use the recent technique of surface plasmon resonance (SPR), in detg. the kinetics of assocn. and dissocn. involved in the interaction of ***endotoxin*** with a few selected ***peptides*** that have structural features resembling PMB. The results, in conjunction with the thermodn. data derived using isothermal titrn. calorimetry (ITC), stress the vital role played by amphiphilicity of the peptides and hydrophobic forces in this biol. important interaction.

L12 ANSWER 5 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Novel synthetic ***peptides*** with antimicrobial and ***endotoxin*** neutralizing properties for management of the sepsis syndrome
AB A peptide with an amino acid compn. such that the ***peptide*** is amphipathic, ***cationic*** and forms a stable .alpha.-helix and has the following structure comprising .gtoreq.12 amino acids: R1-R2-A1-B1-(A2-B2-C1-A3)m-(C2)n-R3, wherein A = an amino acid selected from the basic amino acids Lys, Arg or His; B = an amino acid selected from the arom. amino acids Phe, Trp or Tyr; C = an amino acid selected from the group comprising the hydrophobic amino acids Leu, Ile, Val or Ala; and said peptide has either the orientation according to the formula or the retro orientation thereof, wherein at least 0-n of the repetitive sequence motifs (A2-B2-C1-A3) have the retro orientation and the remaining repetitive motifs (A2-B2-C1-A3) have the orientation as presented in the formula and wherein, R1, R2, and R3 are a no. of amino acids, said no. ranging 0-15 for each of the combination of R1 and R2 and for R3 and wherein m = 1-10, preferably 2-8, more preferably 2-5 and n = 1-3, a pharmaceutical compn. comprising such a peptide application thereof in treatment or diagnosis related to i.a. parasite infection topical and systemic tumors and septic shock.

L12 ANSWER 6 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Interaction of the cyclic antimicrobial ***cationic*** ***peptide*** bactenecin with the outer and cytoplasmic membrane
AB Bactenecin, a 12-amino acid ***cationic*** antimicrobial ***peptide*** from bovine neutrophils, has two cysteine residues, which form one disulfide bond, making it a cyclic mol. To study the importance of the disulfide bond, a linear deriv. Bac2S was made and the reduced form (linear bactenecin) was also included in this study. CD spectroscopy showed that bactenecin existed as a type I .beta.-turn structure regardless of its environment, while the reduced form and linear bactenecin adopted different conformations according to the lipophilicity of the environment. Bactenecin was more active against the Gram-neg. wild type bacteria Escherichia coli, Pseudomonas aeruginosa, and Salmonella typhimurium than its linear deriv. and reduced from, while all three peptides were equally active against the outer membrane barrier-defective mutants of the first two bacteria. Only the two linear peptides showed activity against the Gram-pos. bacteria Staphylococcus epidermidis and Enterococcus faecalis. Bactenecin interacted well with the outer membrane and its higher affinity for E. coli UB1005 lipopolysaccharide and improved ability to permeabilize the outer membrane seemed to account for its better antimicrobial activity against Gram-neg. bacteria. The interaction of bactenecin with the cytoplasmic membrane was detd. by its ability to dissipate the membrane potential by using the fluorescence probe 3,3-dipropylthiacarbocyanine and an outer membrane barrier-defective mutant E. coli DC2. It was shown that the linear deriv. and reduced form were able to dissipate the membrane potential at much lower concns. than bactenecin despite the similar minimal inhibitory concns. of all three against this barrier-defective mutant.

L12 ANSWER 7 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI The ***lipopolysaccharide*** of Bordetella bronchiseptica acts as a protective shield against antimicrobial ***peptides***
AB Resistance profiles of the two Bordetella species B. bronchiseptica and B. pertussis against various antimicrobial peptides were detd. in liq. survival and agar diffusion assays. B. bronchiseptica exhibited higher resistance against all tested peptides than B. pertussis. The most powerful agents acting on B. bronchiseptica were, in the order of their killing efficiencies, cecropin P > cecropin B > magainin-II-amide > protamine > melittin. Interestingly, for B. bronchiseptica, the resistance level was affected by phase variation, as a bvgS deletion deriv. showed an increased sensitivity to these peptides. Tn5-induced protamine-sensitive B. bronchiseptica mutants, which were very susceptible to most of the ***cationic*** ***peptides*** , were isolated. In

two of these mutants, the genetic loci inactivated by transposon insertion were identified as contg. genes highly homologous to the wlbA and wlbL genes of B. pertussis that are involved in the biosynthesis of lipopolysaccharide (LPS). In agreement with this finding, the two ***peptide*** -sensitive mutants revealed structural changes in the ***LPS*** , resulting in the loss of the O-specific side chains and the prevalence of the LPS core structure. Thus, LPS plays a major role in the resistance of B. bronchiseptica against the action of antimicrobial peptides and B. pertussis is much more susceptible to these peptides due to the lack of the highly charged O-specific sugar side chains.

L12 ANSWER 8 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Treatment of ***endotoxin*** -associated disorders with ***cationic*** ***peptides***
AB A method for the microbial prodn. of a ***cationic*** ***peptide***
having anti-microbial activity is provided, wherein the ***cationic*** ***peptide*** is first produced as a fusion protein having an anionic portion for suppressing the antimicrobial activity of the cationic portion. A novel ***cationic*** ***peptide*** having anti-microbial activity and ***LPS*** -binding activity is also provided. Such peptides are useful for suppressing the growth of bacteria and for the treatment of endotoxemia-assocd. disorders.

L12 ANSWER 9 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Polymyxin-B stimulates tumor necrosis factor-.alpha. production by human peripheral blood mononuclear cells
AB Gram-neg. bacterial lipopolysaccharide (LPS) is a well known stimulus for
cytokine prodn., particularly interleukin-1 (IL-1) and tumor necrosis factor .alpha. (TNF.alpha.). Polymyxin B (PMX-B) is a ***cationic*** ***polypeptide*** that binds to ***LPS*** , neutralizing its biol. effects. PMX-B also disrupts gram-neg. bacterial cell membrane phospholipids but is highly toxic to mammalian cells, therefore is of limited use. PMX-B is used as additive to media, as a way to handle LPS contamination. To derive benefit from the ability of PMX-B to neutralize lipid A in vivo while avoiding its systemic toxicity, PMX-B was covalently bound to polystyrene-deriv. fibers, creating a hemoperfusion column (PMX-F) for the selective removal of circulating endotoxin (ET). In vitro PMX-F hemoperfusion studies have demonstrated effective ET removal, using
either the Limulus amebocyte lysate assay or TNF.alpha. prodn. by peripheral blood mononuclear cells (PBMC) as an index of ET removal. However, the question whether PMX-B itself could stimulate human PBMC to
produce cytokines has not been adequately addressed. The authors examd. the effect of increasing concns. of PMX-B on cytokine prodn. by PBMC in vitro. PBMC harvested from healthy volunteers were incubated for 24 h at 37.degree. with control (tissue culture media RPMI), or 5 .mu.g/mL, 10 .mu.g/mL, 20 .mu.g/mL or 100 .mu.g/mL PMX-B. At the end of 24 h, PBMC
were subjected to three freeze-thaw cycles, and total TNF.alpha. prodn. (pg/2.5.times.106 PBMC) was measured by RIA. Total TNF.alpha. prodn. by
PBMC was 163 pg, 171 pg, 164 pg, 323 pg and 331 pg, in the control, PMX-B
5 .mu.g/mL, 10 .mu.g/mL, 20 .mu.g/mL and 100 .mu.g/mL conditions, resp. Compared to controls (RPMI), the percentage increase in TNF.alpha. prodn. by PBMC was 5%, 1%, 99% and 103% in the presence of 5 .mu.g/mL, 10 .mu.g/mL, 20 .mu.g/mL and 100 .mu.g/mL of PMX-B, resp. Furthermore, total
TNF.alpha. prodn. correlated significantly with increasing concns. of PMX-B (R=0.53). The authors conclude that the use of PMX-B in in vitro studies as an LPS-neutralizing agent, or in the exptl. treatment of endotoxic or septic shock can lead to erroneous interpretations of cytokine prodn. by PBMC, and should be used cautiously in in vitro systems at high concns.

L12 ANSWER 10 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI The therapeutic potential of ***cationic*** ***peptides***
AB A review with 30 refs. Novel classes of antibiotics that are useful against resistant bacteria are a major need in human medicine. ***Cationic*** antimicrobial ***peptides*** are utilized as nature's antibiotics, being produced constitutively or in response to infection in virtually every type of organism, from plants and insects to man. Thus, these peptides are now being considered as potential antibiotics for infections. They have the following assets: structural diversity, rapid bactericidal action, a broad spectrum of activity that includes most of the clin. important resistant pathogens, and several ancillary activities which can include antifungal, antiviral, and antiendotoxin activities, and promotion of wound healing. ***Cationic*** ***peptides*** and proteins are now proceeding through clin. trials as topical antibiotics and antiendotoxins.

L12 ANSWER 11 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Removal of cytokine inducing substances by polymyxin-B immobilized polystyrene-derivative fibers during in vitro hemoperfusion of 10% human plasma containing Staphylococcus aureus challenge
AB Staphylococcus aureus (S. aureus) is frequently isolated from blood cultures in the hospital setting. The pathogenesis of S. aureus bacteremia probably replicates mechanisms implicated in gram neg. bacterial infections. Cell wall components, such as peptidoglycans and lipoteichoic acids (LTA), can trigger cytokine prodn. Polymyxin-B (PMX-B)
is a ***cationic*** ***peptide*** that binds ***endotoxin*** (ET) and inhibits its activity. Based on this principle, PMX-B was incorporated in polystyrene-deriv. fibers, creating a hemoperfusion column (PMX-20R) that removes ET. The authors assessed whether S. aureus possesses PMX-B suppressible cytokine-inducing substances, and whether LTA, an anionic mol., is one such substance. Heparinized blood was obtained from healthy volunteers, peripheral blood mononuclear cells (PBMC) were isolated by Ficoll-Hypaque sepn., and 10% human plasma prepd.
PBMC were incubated with 1, 5, or 10 .mu.g/mL of S. aureus LTA, with and
without 10 .mu.g/mL of PMX-B. Also, using PMX-20R, in vitro hemoperfusion
(IVH) was performed with 10% human plasma contg. a 1:1,000 diln. of S. aureus challenge at 100 mL/min for 2 h at 37.degree.C, and plasma obtained before and after IVH was incubated with PBMC. After a 24 h incubation at 37.degree.C, PBMC were subjected to three freeze-thaw cycles, and total TNF.alpha. was measured by RIA. TNF.alpha. prodn. by PBMC incubated with
LTA was 164 .+-. 4 pg, 324 .+-. 54 pg, 657 .+-. 55 pg, and 1143 .+-. 215 pg in control, and LTA 1, 5, and 10 .mu.g/mL, resp. The addn. of PMX-B resulted in a 40 .+-. 12% ($p = 0.02$), 61 .+-. 6% ($p = 0.002$), and 62 .+-. 14% ($p = 0.02$) decrease in TNF.alpha. prodn., resp. Before IVH, TNF.alpha. prodn. by PBMC incubated with 10% plasma contg. S. aureus challenge was 1275 .+-. 70 pg. After 2 h of IVH, the decrease in TNF.alpha. prodn. was 20 .+-. 4% ($p = 0.002$). In conclusion, S. aureus LTA induces TNF.alpha. prodn. that is significantly suppressed by PMX-B. Consequently, S. aureus cytokine-inducing substances are removed during IVH with PMX-20R, and this may be due to stoichiometric binding of LTA to
PMX-B.

L12 ANSWER 12 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Regulation of polymyxin resistance and adaptation to low-Mg2+ environments
AB The PmrA-PmrB two-component system of Salmonella typhimurium controls
resistance to the peptide antibiotic polymyxin B and to several antimicrobial proteins from human neutrophils. Amino acid substitutions in the regulatory protein PmrA conferring resistance to polymyxin lower the overall neg. charge of the ***lipopolysaccharide*** (***LPS***), which results in decreased bacterial binding to ***cationic*** ***polypeptides*** and increased bacterial survival within human neutrophils. We have now identified three PmrA-activated loci that are required for polymyxin resistance. These loci were previously shown to be necessary for growth on low-Mg2+ solid media, indicating that LPS modifications that mediate polymyxin resistance are responsible for the adaptation to Mg2+-limited environments. Conditions that promote transcription of PmrA-activated genes-growth in mildly acidic pH and micromolar Mg2+ concns.-increased survival in the presence of polymyxin over 16,000-fold in a wild-type organism but not in a mutant lacking pmrA. Our expts. suggest that low pH and low Me2+ concns. may induce expression
of PmrA-activated genes within phagocytic cells and promote bacterial resistance to host antimicrobial proteins. We propose that the LPS is a Mg2+ reservoir and that the PmrA-controlled LPS modifications neutralize surface neg. charges when Mg2+ is transported into the cytoplasm during growth in Mg2+-limited environments.

L12 ANSWER 13 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Neutralization of the in vivo activity of E. coli-derived ***lipopolysaccharide*** by ***cationic*** ***peptides***
AB A review 25 with refs. on materials and procedures useful for the in vivo study of the ***lipopolysaccharide*** neutralization potential of

neutrophil-derived ***cationic*** ***peptides*** (such as CAP37, CAP57, and CAP18) in rats. Biol. and physiol. responses in rats are assessed in the testing.

L12 ANSWER 14 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Antimicrobial ***cationic*** ***peptides***
AB A novel class of 25 ***cationic*** ***peptides*** , called bactolysins, is provided which have antimicrobial activity and have the ability to significantly reduce the level of lipopolysaccharide-induced tumor necrosis factor. Examples of such peptides include NH2-KWKSFIKKLTTAVKKVLTTGLPALIS-COOH and NH2-KWKSFIKKLTSAAKKVVTTAKPLISS-COOH. These peptides are useful for inhibiting microbial infection or growth, as well as reducing the effects of endotoxemia and are often synergistic with conventional antibiotics and/or lysozyme. In addnl., bactolysins are useful as antifungal agents, antitumor agents, or antiviral agents.

L12 ANSWER 15 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI A derivative of cationic antimicrobial protein attenuates lung injury by suppressing cell adhesion
AB Cationic antimicrobial protein of 18 kD (CAP18) was identified and purified from rabbit granulocytes and shown to inhibit various activities of lipopolysaccharide (LPS). We investigated the effect of a 32-amino acid C-terminal fragment of CAP18 (CAP18-derived peptide, CDP) on the pathogenesis of acute lung injury caused by i.v. endotoxin. Guinea pigs were divided into six groups: (1) saline control (n = 8), (2) CDP-alone (n = 8), (3) LPS-alone (n = 8), (4) LPS+CDP0m (n = 8), (5) LPS+CDP10m (n = 8), and (6) LPS+CDP60m (n = 8). A CDP dose of 0.2 mg/kg was injected at various time points after LPS injection. Lung wet-to-dry wt. ratio, [125I]albumin leakage in lung tissue and bronchoalveolar lavage (BAL) fluid, differential cell count in BAL fluid, and histopathol. features were examd. 4 h after i.v. administration of 0.02 mg/kg of LPS. The LPS+CDP0m and the LPS+CDP10m groups showed significantly attenuated lung injury compared to that seen in the LPS-alone group, however the LPS+CDP60m group revealed no attenuation of lung injury. The accumulation of peripheral white blood cells into pulmonary vasculature was attenuated only in the LPS+CDP0m but not in the LPS+CDP10m groups. We examd. the effect of CDP on the expression of adhesion mols. using human umbilical vein endothelial cells, the result of which showed that CDP suppressed the LPS-induced expression of adhesion mols. in a dose-dependent manner. We conclude that CDP attenuates inflammatory cell migration into alveoli resulting in the attenuation of lung injury.

L12 ANSWER 16 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Antiendotoxin activity of ***cationic*** ***peptide*** antimicrobial agents
AB The endotoxin from gram-neg. bacteria consists of a mol. lipopolysaccharide (LPS) which can be shed by bacteria during antimicrobial therapy. A resulting syndrome, endotoxic shock, is a leading cause of death in the developed world. Thus, there is great interest in the development of antimicrobial agents which can reverse rather than promote sepsis, esp. given the recent disappointing clin. performance of antiendotoxin therapies. We describe here two small ***cationic*** ***peptides*** , MBI-27 and MBI-28, which have both antiendotoxic and antibacterial activities in vitro and in vivo in animal models. We had previously demonstrated that these ***peptides*** bind to ***LPS*** with an affinity equiv. to that of polymyxin B. Consistent with this, the ***peptides*** blocked the ability of ***LPS*** and intact cells to induce the endotoxic shock mediator, tumor necrosis factor (TNF), upon incubation with the RAW 264.7 murine macrophage cell line. MBI-28 was equiv. to polymyxin B in its ability to block LPS induction of TNF by this cell line, even when added 60 min after the TNF stimulus. Furthermore, MBI-28 offered significant protection in a galactosamine-sensitized mouse model of lethal endotoxic shock. This protection correlated with the ability of MBI-28 to reduce LPS-induced circulating TNF by nearly 90% in this mouse model. Both MBI-27 and MBI-28 demonstrated antibacterial activity against gram-neg. bacteria in vitro and in vivo against Pseudomonas aeruginosa infections in neutropenic mice.

L12 ANSWER 17 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Manufacture with microorganisms of ***LPS*** -binding antibacterial ***cationic*** ***peptides*** conjugated with anionic ***peptides***
AB A method for the microbial prodn. of a ***cationic*** ***peptide*** having anti-microbial activity is provided, wherein the ***cationic*** ***peptide*** is first produced as a fusion protein having an anionic portion for suppressing the anti-microbial activity of the cationic portion. A novel ***cationic*** ***peptide*** having anti-microbial activity and ***LPS*** -binding activity is also provided. Such peptides are useful for suppressing the growth of bacteria and for the treatment of endotoxemia-assocd. disorders. Chimeric genes for synthetic peptides CEME and CEMA (based on cecropin and melittin) fused to a glutathione S-transferase fragment were expressed in Escherichia coli and Staphylococcus aureus. The peptides permeabilized the membranes of Pseudomonas aeruginosa and Enterobacter cloacae. They were able to kill a broad range of Gram-neg. bacteria with MIC's of 1-16 .upsilon.g/mL. CEME and CEMA bound to LPS and inhibited LPS-mediated tumor necrosis factor induction in macrophages. In a mouse endotoxic shock model, the ***peptides*** protected the mice from ***LPS*** endotoxicity.

L12 ANSWER 18 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Brucella-Salmonella lipopolysaccharide chimeras are less permeable to hydrophobic probes and more sensitive to ***cationic*** ***peptides*** and EDTA than are their native Brucella sp. counterparts
AB A rough (R) Brucella abortus 45/20 mutant was more sensitive to the bactericidal activity of polymyxin B and lactoferricin B than was its smooth (S) counterpart but considerably more resistant than Salmonella montevideo. The outer membrane (OM) and isolated lipopolysaccharide (***LPS***) of S. montevideo showed a higher affinity for these ***cationic*** ***peptides*** than dit the corresponding B. abortus OM and ***LPS*** . We took advantage of the moderate sensitivity of R B. abortus to ***cationic*** ***peptides*** to construct live R B. abortus-S- ***LPS*** chimeras to test the activities of polymyxin B, lactoferricin B, and EDTA. Homogeneous and abundant peripheral distribution of the heterologous S-LPS was obsd. on the surface of the chimeras, and this coating had no effect on the viability or morphol. of the cells. When the heterologous LPS corresponded to the less sensitive bacterium S B. abortus S19, the chimeras were more resistant to ***cationic*** ***peptides*** ; in contrast, when the S- ***LPS*** was from the more sensitive bacterium S. montevideo, the chimeras were more susceptible to the action of peptides and EDTA. A direct correlation between the amt. of heterologous S- ***LPS*** on the surface of chimeric Brucella cells and ***peptide*** sensitivity was obsd. Whereas the damage produced by polymyxin B in S. montevideo and B.abortus-S. montevideo S-LPS chimeras was manifested mainly as OM blebbing and inner membrane rolling, lactoferricin B caused inner membrane detachment, vacuolization, and the formation of internal electron-dense granules in these cells. Native S and R B. abortus strains were permeable to the hydrophobic probe N-phenyl-1-naphthylamine (NPN). In contrast, only reduced amts. of NPN partitioned into the OMs of the S. montevideo and B. abortus-S. montevideo S-LPS chimeras. Following peptide exposure, accelerated NPN uptake similar to that obsd. for S. montevideo was detected for the B. abortus-S. montevideo LPS chimeras. The partition of NPN into native or EDTA-, polymyxin B-, or lactoferricin B-treated LPS micelles of S. montevideo or B. abortus mimicked the effects obsd. with intact cells, and this was confirmed by using micelle hybrids of B. abortus and S. montevideo LPSs. The results showed that LPS is the main cause of B. abortus' resistance to bactericidal ***cationic*** ***peptides*** , the OM-disturbing action of divalent cationic chelants, and OM permeability to hydrophobic substances. It is proposed that these three features are related to the ability of Brucella bacteria to multiply within phagocytes.

L12 ANSWER 19 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI The outer membranes of Brucella spp. are resistant to bactericidal ***cationic*** ***peptides***
AB The actions of polymyxin B, rabbit polymorphonuclear lysosome exts., 14 polycationic peptides (including defensin NP-2, cecropin P1, lactoferricin B, and active ***peptides*** from ***cationic*** protein 18 and bactenecin), EDTA, and Tris on Brucella spp. were studied, with other

gram-neg. bacteria as controls. Brucella spp. were comparatively resistant to all of the agents listed above and bound less polymyxin B, and their outer membranes (OMs) were neither morphol. altered nor permeabilized to lysozyme by polymyxin B concns., although both effects were obsd. for controls. EDTA and peptides increased or accelerated the participation of the hydrophobic probe N-phenyl-naphthylamine into Escherichia coli and Haemophilus influenzae OMs but had no effect on Brucella OMs. Since Brucella and H. influenzae OMs are permeable to hydrophobic compds., the results show that such unusual permeability is not necessarily related to resistance to polycations. Although rough (R) B. abortus and B. ovis were more resistant than the controls were, there were qual. and quant. differences with smooth (S) brucellae; this may explain known host range and virulence differences. Brucella S-lipopolysaccharides (LPSs) had reduced affinities for polycations, and insertion of brucella and Salmonella montevideo S-LPSs into the OM of a Brucella R- ***LPS*** mutant increased and decreased, resp., its resistance to ***cationic*** ***peptides*** . The results show that the core lipid A of Brucella LPS plays a major role in polycation resistance and that O-chain d. also contributes significantly. It is proposed that the features described above contribute to Brucella resistance to the oxygen-independent systems of phagocytes.

L12 ANSWER 20 OF 38 CAPLUS COPYRIGHT 1999 ACS

TI Improvement of outer membrane-permeabilizing and ***lipopolysaccharide*** -binding activities of an antimicrobial ***cationic*** ***peptide*** by C-terminal modification

AB Antimicrobial ***cationic*** ***peptides*** have been discovered in many different organisms and often possess a broad range of activity. In this study, the mechanisms of actions of melittin and 2 synthetic peptides, CEME (a cecropin-mellitin hybrid) and CEMA, were investigated against gram-neg. bacteria. CEMA was produced by recombinant DNA procedures and is an analog of CEME with a modified C terminus resulting in 2 addnl. pos. charges. All 3 peptides showed good antimicrobial activity against 4 different gram-neg. bacteria, but only CEMA somewhat augmented the activity of some conventional antibiotics in synergy studies. Studies using the bacteria Pseudomonas aeruginosa and Enterobacter cloacae showed that the peptides all permeabilized bacterial outer membranes to the hydrophobic fluorophor 1-N-phenylnaphthylamine and the protein lysozyme, with CEMA being the most active. CEMA also had the strongest relative binding affinity for bacterial endotoxin (lipopolysaccharide). These data collectively indicated that these peptides all cross the outer membrane by the self-promoted uptake pathway and that CEMA is the peptide most effective at accessing this pathway.

L12 ANSWER 21 OF 38 CAPLUS COPYRIGHT 1999 ACS

TI Molecular cloning of a putative homolog of proline/arginine-rich antibacterial peptides from porcine bone marrow

AB Screening of a porcine bone marrow cDNA library with a PCR-derived probe from rabbit LPS-binding protein CAP18 led to the discovery of two closely related clones. The longer, full-length cDNA clone encodes a 228 amino acid residue protein similar to the family of antibacterial/ ***LPS*** -binding ***cationic*** ***peptides*** . In contrast to other hitherto discovered precursors of Pro/Arg-rich peptides from this family, they have a novel, unique structure of the C-terminal region of 100 amino acid residues with a repeating sequence of ten residues (FPPPNXPGPR, where X = V or F). These precursors could represent a part of the antibacterial peptide repertoire of porcine bone marrow.

L12 ANSWER 22 OF 38 CAPLUS COPYRIGHT 1999 ACS

TI Gene therapy by intramuscular injection of plasmid DNA: Studies on firefly luciferase gene expression in mice

AB Direct injection of nonviral, covalently closed circular plasmid DNA into muscle results in expression of the DNA in myofiber cells. The authors have examd. the expression of firefly luciferase DNA constructs injected into adult murine skeletal muscle. Considerable variation in luciferase enzyme expression was noted among constructs with different regulatory elements, among different batches of the same DNA construct, and among similar transfection expts. performed at different times. This variation was minimized by using single batches of plasmid DNA and by performing comparable sets of expts. concurrently. A quant. exptl. protocol was defined for comparing various aspects of the transfection process. The authors report that a luciferase construct contg. the human cytomegalovirus immediate-early gene promoter plus intron A (a construct termed "p-CMVint-lux") showed the highest expression among several constructs tested. Dose-response and time course analyses of p-CMVint-lux DNA injections showed that maximal luciferase expression was achieved with 25 .mu.g of DNA at 7-14 days post-injection. Selected manipulations of the transfection process were examd. for their influence on luciferase expression. Variations in the rate of DNA injection, needle size, injection vol., and vehicle temp. had no significant effect on luciferase expression. The presence of ***endotoxin*** , ***cationic*** ***peptide*** , muscle stimulants or relaxants, vasoconstrictors, metal chelators, or lysosomal lytic reagents had no significant effect on expression. However, linearization of the DNA, injection of the DNA in water rather than saline, or inclusion of a DNA intercalating agent nearly abolished luciferase expression. And finally, increasing the injection dose by giving multiple injections over a 10-day period increased expression proportionally to the no. of injections.

L12 ANSWER 23 OF 38 CAPLUS COPYRIGHT 1999 ACS

TI Interaction of basic amphiphilic polypeptide antimicrobials, gramicidin S, tyrocidine and efrapeptin, with endotoxic lipid A

AB Gramicidin S, tyrocidine and efrapeptin, basic hydrophobic peptide antimicrobials, bind lipid A with apparent Kds of 1.68 .mu.M, 2.65 .mu.M and 4.92 .mu.M resp., and inhibit lipid A activity in the Limulus amebocyte lysate gelation and splenocyte proliferation assays. The results suggest that ***endotoxin*** binding properties may be a general property of ***cationic*** amphiphilic ***peptides*** .

L12 ANSWER 24 OF 38 CAPLUS COPYRIGHT 1999 ACS

TI Interactions between magainin 2 and Salmonella typhimurium outer membranes: effect of lipopolysaccharide structure

AB The role of the outer membrane and ***lipopolysaccharide*** (***LPS***) in the interaction between the small ***cationic*** antimicrobial ***peptide*** magainin 2 and the gram-neg. cell envelope was studied by FT-IR spectroscopy. Magainin 2 alters the thermotropic properties of the outer membrane-peptidoglycan complexes from wild-type S. typhimurium and a series of LPS mutants which display differential susceptibility to the bactericidal activity of cationic antibiotics. These results are correlated with the LPS phosphorylation pattern and charge (characterized by high-resoln. 31P NMR) and outer membrane lipid compn., and are compared to the bactericidal susceptibility. LPS mutants show a progressive loss of resistance to killing by magainin 2 as the length of the LPS polysaccharide moiety decreases. Disordering of the outer membrane lipid fatty acyl chains by magainin 2, however, depends primarily upon the magnitude of LPS charge rather than the length of the LPS polysaccharide, contradicting the proposal by J. Weiss et al. (1980) that the sugar side chain of LPS shields the neg. charges of the outer membrane surface. While disruption of outer membrane structure most likely is not the primary factor leading to cell death, the susceptibility of gram-neg. cells to magainin 2 is assocd. with factors that facilitate the transport of the peptide across the outer membrane, such as the magnitude and location of LPS charge, the concn. of LPS in the outer membrane, outer membrane mol. architecture, and the presence or absence of the O-antigen side chain.

L12 ANSWER 25 OF 38 CAPLUS COPYRIGHT 1999 ACS

TI Primary structures and functions of anti- ***lipopolysaccharide*** factor and tachyplesin ***peptide*** found in horseshoe crab hemocytes

AB The amino acid sequence is presented for tachyplesin, a ***cationic*** ***peptide*** isolated from Japanese horseshoe crab hemocytes. Tachyplesin was compared to a previously isolated and characterized anti-lipopolysaccharide factor. The most probable function of tachyplesin is antimicrobial for the defense of the horseshoe crab against microbial infections.

L12 ANSWER 26 OF 38 CAPLUS COPYRIGHT 1999 ACS

TI Interactions between Salmonella typhimurium ***lipopolysaccharide*** and the antimicrobial ***peptide*** , magainin 2 amide

AB Effects of magainin 2 amide on the phase behavior of S. typhimurium lipopolysaccharide were characterized by FT-IR spectroscopy. This antimicrobial ***cationic*** ***peptide*** disorders the ***lipopolysaccharide*** at mol. ratios of ***lipopolysaccharide*** to magainin >4, and can induce a temp.-dependent structural reorientation. The nature of the 5 phosphate groups of lipopolysaccharide was detd. by 31P NMR spectroscopy. At pH 7.4, the net charge on the phosphates is -7. Lipopolysaccharide undoubtedly plays an important role in modulating the interactions of magainin with the gram-neg. cell envelope and may act as a mol. sponge to protect the plasma membrane.

L12 ANSWER 27 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Outer membrane structure in smooth and rough strains of Salmonella typhimurium and their susceptibility to the antimicrobial peptides, magainins and defensins
AB The fluidity of the outer membranes and extd. lipopolysaccharides of smooth S. typhimurium and 6 rough mutants and the thermotropic behavior of
the lipopolysaccharides were detd. The structures of the ***cationic*** antibacterial ***peptides*** , the defensins and magainins, are discussed. The rough mutants of S. typhimurium are more susceptible to these peptides, and the degree of susceptibility is proportional to the decrease in the amt. of carbohydrate in the lipopolysaccharide. By studying structural alterations in both the membranes and peptides as binding occurs, insight will be gained into the microbicidal action of the peptides.

L12 ANSWER 28 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Polymyxin B suppresses the stimulating effect of pertussis vaccine on hematopoiesis in mice
AB Killed whole-cell pertussis vaccine (PV) prepd. from formol-treated Bordetella pertussis had a stimulating effect on hematopoiesis in mice. This effect was manifested by increased nos. of endogenous colonies developing in the spleen of mice on days 5 and 9 after sublethal irradn., by sharp stimulation of the proliferative activity of splenic colony-forming units (CFUs) originating in the bone marrow, and by the elevated CFU level in the peripheral blood. Preincubation of the whole-cell PV with polymyxin B, a ***cationic*** ***polypeptide*** selectively reacting with the lipid A moiety of ***lipopolysaccharides*** (***LPS***), sharply decreased the hematopoietic effect of the vaccine, while incubation with Cetavlon, a cationic detergent which interacts with the polysaccharide moiety of LPS, had no effect on the ability of the vaccine to stimulate hematopoiesis. The stimulating effect of whole-cell PV on hematopoiesis is supposedly due to the lipid A moiety of LPS.

L12 ANSWER 29 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Endotoxin-polymyxin complexes in an improved enzyme-linked immunosorbent
assay for IgG antibodies in blood donor sera to gram-negative endotoxin core glycolipids
AB Common or cross-reactive epitopes of gram-neg. endotoxins are found in the
inner core glycolipid region of the outer membrane lipopolysaccharides (LPS). Hydrophobic LPS from rough mutants of gram-neg. bacteria, lacking serotype polysaccharide O-antigen chains, did not bind satisfactorily to polystyrene microplates for ELISA detection of cross-reactive IgG anti-endotoxin antibodies. When these ***LPS*** mols. were reacted with the ***cationic*** ***polypeptide*** polymyxin B, complexes were formed which were stable when coated on microplates.
LPS-polymyxin
complexes allowed optimization of conditions for an ELISA for IgG antibodies to the core glycolipid region of endotoxins which could be used for screening large nos. of blood donor sera.

L12 ANSWER 30 OF 38 CAPLUS COPYRIGHT 1999 ACS
TI Dose-dependent reduction of lipopolysaccharide pyrogenicity by polymyxin B
AB Polymyxin B (PB) [1404-26-8], a ***cationic*** ***polypeptide***
antibiotic, binds lipid A, the active moiety of ***lipopolysaccharide*** (***LPS***), with high affinity and abrogates several biol. responses to LPS. The effect of PB on the pyrogenicity of purified LPS from Escherichia coli 0111:B4 was studied in rabbits. PB reduced the pyrogenic response to LPS in a dose-dependent manner at mass ratios (PB:LPs) from 5:1 to 100:1. Previous PB was effective only at much higher doses, but PB itself is pyrogenic, unless previously .gamma.-irradiated. Results confirm in vivo the anti-endotoxic action of PB.

L12 ANSWER 31 OF 38 MEDLINE
TI Tachyplesin, a class of antimicrobial peptide from the hemocytes of the horseshoe crab (Tachypleus tridentatus). Isolation and chemical structure.
AB A ***cationic*** ***peptide*** , designated tachyplesin, was isolated from acid extracts of horseshoe crab (Tachypleus tridentatus) hemocyte debris. It consists of 17 residues and the structure determined by Edman degradation is: (formula; see text) The carboxyl-terminal end of this peptide was identified as arginine alpha-amide, and the whole sequence including the alpha-amide was also confirmed by fast atom bombardment mass spectrometry, indicating a mass value of 2263. Tachyplesin inhibits growth of both Gram-negative and -positive bacteria at low concentrations and formed a complex with bacterial ***lipopolysaccharide*** . Tachyplesin seems likely to act as antimicrobial ***peptide*** for self-defense in the horseshoe crab against invading microorganisms.

L12 ANSWER 32 OF 38 BIOSIS COPYRIGHT 1999 BIOSIS
TI Protective effects of a human 18-kilodalton cationic antimicrobial protein (CAP18)-derived peptide against murine endotoxemia.
AB CAP18 (an 18-kDa cationic antimicrobial protein) is a granulocyte-derived
protein that can bind lipopolysaccharide (LPS) and inhibit various activities of LPS in vitro. The present study examined the protective effect of a synthetic 27-amino-acid ***peptide*** (CAP18109-135) from the ***LPS*** -binding domain of CAP18 against antibiotic-induced endotoxin shock, using highly LPS-sensitive D-(+)-galactosamine (D-GalN)-sensitized C3H/HeN mice. The antibiotic-induced endotoxin (CAZ-endotoxin) was prepared from the culture filtrate of Pseudomonas aeruginosa PA01 exposed to ceftazidime (CAZ). Injection of CAP18109-135
protected the mice injected with LPS or CAZ-endotoxin from death and lowered their tumor necrosis factor (TNF) levels in serum in a dose-dependent manner. Treatment with CAZ caused death of the D-GalN-sensitized P. aeruginosa PAO-infected mice within 48 h, while injection with CAP18109-135 rescued the mice from death. In the mice rescued from death by injection with CAP18109-135 endotoxin levels in plasma and TNF production by liver tissues were decreased but the numbers of viable infecting bacteria in their blood were not decreased significantly and remained at the levels in CAZ-treated mice. These results indicate that CAP18109-135 is capable of preventing antibiotic-induced endotoxic shock in mice with septicemia and that the effect is due to its LPS-neutralizing activity rather than to its antibacterial activity.

L12 ANSWER 33 OF 38 BIOSIS COPYRIGHT 1999 BIOSIS
TI ***Peptides*** corresponding to ***cationic*** sequences of ***LPS*** -binding proteins inhibit ***endotoxin*** -induced responses.

L12 ANSWER 34 OF 38 BIOSIS COPYRIGHT 1999 BIOSIS
TI Neutralization of the in vivo activity of E. coli-derived ***lipopolysaccharide*** by ***cationic*** ***peptides*** .

L12 ANSWER 35 OF 38 BIOSIS COPYRIGHT 1999 BIOSIS
TI Comparison of structurally related ***cationic*** ***peptides*** in their ability to neutralize the biological activity of ***endotoxin*** .

L12 ANSWER 36 OF 38 BIOSIS COPYRIGHT 1999 BIOSIS
TI INDUCTION OF ***CATIONIC*** ***PEPTIDES*** IN RABBIT ALVEOLAR
MACROPHAGE BY IMMUNOMODULATORS AND CYTOKINES.

L12 ANSWER 37 OF 38 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
TI Neutralization of the hemodynamic effects of endotoxin by polymyxin B.
AB Observations that the cyclic ***cationic*** ***polypeptide*** antibiotics interfere with a number of biologic actions of ***endotoxin*** prompted this study of the influence of polymyxin B on endotoxin induced changes of blood pressure, cardiac index, and systemic vascular resistance in the anesthetized dog. There were 4 experimental groups consisting of dogs given saline solution, endotoxin, polymyxin B, or endotoxin mixed with polymyxin B prior to administration. At 1.5 hr after treatment the dogs treated with endotoxin exhibited marked hypotension, with a corresponding decline in cardiac index and calculated systemic vascular resistance. The dogs treated with saline solution and polymyxin B and endotoxin plus polymyxin B sustained similar decreases in cardiac index but maintained blood pressure through an elevation in the calculated systemic vascular resistance. Those treated with endotoxin mixed with polymyxin B were able to sustain blood pressure through elevation of the systemic vascular resistance in a manner not unlike that seen in the saline solution and polymyxin B treated dogs. While the data do not explain the nature of the interaction, they reflect yet another antibiotic endotoxin interaction which may be useful in further definition of the active sites of the endotoxin molecule and localization of the endotoxin target cells of the host. It is also possible that the cyclic ***cationic*** ***polypeptide*** antibiotics will prove to have useful therapeutic properties in addition to their antimicrobial actions.

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FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, SCISEARCH'
ENTERED AT 12:43:41 ON
23 SEP 1999
E PORRO M/AU
L1 205 S E3-E9,E13
L2 51 S L1 AND (PEPTIDE? OR POLYPEPTIDE? OR LPS OR
LIPOPOLYSACCHARIDE
L3 27 S L1 AND ENDOTOXIN?
L4 51 S L2 OR L3
L5 29 DUPLICATE REMOVE L4 (22 DUPLICATES REMOVED)
L6 17 S L5 AND (ENDOTOXIN? OR LPS OR
LIPOPOLYSACCHARIDE?)
L7 2388 S (ENDOTOXIN? OR LPS OR
LIPOPOLYSACCHARIDE?)(10N)(PEPTIDE? OR P
L8 7 S L7 AND SAEP?
L9 5 S L8 NOT L6
L10 97 S L7 AND (CATIONIC(3N)(PEPTIDE? OR POLYPEPTIDE?))
L11 38 DUPLICATE REMOVE L10 (59 DUPLICATES REMOVED)
L12 38 S L11 NOT L6